

Appl. No. 10/516,586  
Amdt. Dated March 12, 2009  
Reply to Office Action of December 23, 2008

Attorney Docket No. 81844.0053  
Customer No.: 26021

### REMARKS

This application has been carefully reviewed in light of the Office Action dated December 23, 2008. Claims 1-18 remain in this application. Claim 1 is the independent Claim. It is believed that no new matter is involved in the amendments or arguments presented herein. Reconsideration and entrance of the amendment in the application are respectfully requested.

### Information Disclosure Statement:

The information disclosure statement filed August 8, 2005 is objected to for failing to comply with 37 C.F.R. § 1.98(a)(2) for not providing a legible copy of the cited foreign patent document JP 63-115572. In response, Applicant encloses herewith a legible copy of JP 63-115572 for consideration by the Office.

### Double Patenting

Claims 1-3, 6, 7, 9 and 16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-3, 5-7 and 9-11 of copending Application No. 11/718,386.

In response, Applicant respectfully requests the rejection be held in abeyance until the allowance of claims.

### Art-Based Rejections

Claims 1-7 and 9-18 were rejected under 35 U.S.C. § 103(a) as obvious over Jap. Pub. No. JP 07-136256 (Inama) in view of U.S Patent U.S. No. 4,576,928 (Tani); Claim 8 is rejected as obvious over Inama in view of U.S. Patent No. 5,286,449 (Kuroda '449) in view of Tani; Claims 1-4, 6-12 and 18 are rejected as obvious over Kuroda in view of Tani; Claims 5 and 13-17 are rejected as obvious over Kuroda in view of Tani.

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and U.S. Patent No. 4,627,915 (Kuroda '915); Claims 1-6 and 9-16 are rejected as obvious over Tani; Claims 7, 8, 17 and 18 are rejected as obvious over Tani in view of Kuroda '449).

Applicant respectfully traverses the rejections and submits that the claims herein are patentable in light of the clarifying amendments above and the arguments below.

#### **The Inama Reference**

Inama is directed to a molecular weight of a ligand is 50,000 or less, and a range of a negative functional group is provided. The molecular weight of a ligand may be any and especially regulation is unnecessary. (See *Inama*; Paragraphs [0009] and [0014]).

#### **The Tani Reference**

Tani is directed to varying viscosity and sulfur content of dextran sulfate and the immobilization of polyanion compound on a column volume of adsorbent (See *Tani*; Col. 6, lines 8-14 and Col. 7, lines 26-46).

#### **The Kuroda '449 Reference**

Kuroda '449 is directed to a weight average molecular weights of a hydrophobic compounds and polyanion compounds (See *Kuroda '449*; Col. 10, lines 9-65).

#### **The Kuroda '915 Reference**

Kuroda '915 is directed to an adsorbent with a negative charge-producing member adapted to produce an effective number of negative charges in a body fluid (See *Kuroda '915*; Abstract).

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**The Claims are Patentable Over the Cited References**

The present application is generally directed to an adsorbent for adsorbing low-density lipoproteins and fibrinogen in a body fluid.

As defined by independent Claim 1, an adsorbent capable of whole blood treatment for adsorbing low-density lipoproteins and fibrinogen is provided. The adsorbent includes a tryptophan derivative and a polyanionic compound which are immobilized on a water-insoluble porous carrier. The amount of the immobilized polyanionic compound is 0.10  $\mu$ mol to 1.5  $\mu$ mol per milliliter of wet volume of the adsorbent. The molar ratio of the amount of the immobilized tryptophan derivative to the amount of the immobilized polyanionic compound is 1 to 70.

The applied references do not disclose or suggest the features of the present invention as defined by independent Claim 1. In particular, the applied references do not disclose or suggest, "the molar ratio of the amount of the immobilized tryptophan derivative to the amount of the immobilized polyanionic compound is 1 to 70," as required by independent Claim 1 of the present invention.

Page 3, 6 and 7 of the Action concedes that Inama, Kuroda '449 and Tani do not disclose that the molar ratio of tryptophan to polyanionic compound is 1 to 70, but asserts that such feature is obvious, as it is not inventive to discover the optimum or workable ranges through routine experimentation.

In particular, M.P.E.P. § 2144.05 (II)(B) states "[a] particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977) (The claimed wastewater treatment device had a tank volume to contractor area of 0.12 gal./sq. ft. The prior art did not recognize that treatment capacity is a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result- effective variable.)."

Likewise, the cited references fail to recognize that adsorption of low-density lipoproteins and fibrinogen is a function of a molar ratio between an amount of immobilized tryptophan and amount of immobilized polyanionic compound (See Specification; Page 12, line 21 to Page 13, line 15 and Page 14, lines 3-14). At best, the references merely teach the disclosure of the molecular weights of the compounds individually, without recognition of the importance of the relationship of the amounts between them.

Tani is directed to varying viscosity and sulfur content of dextran sulfate and the immobilization of polyanion compound on a column volume of adsorbent (See Tani; Col. 6, lines 8-14 and Col. 7, lines 26-46).

Kuroda '449 teaches weight average molecular weights of a hydrophobic compound and polyanion compound individually (See Kuroda '449; Col. 10, lines 9-65). Weight average molecular weight does not teach the amount of compound used, and is a characteristic of the compound, regardless of the amount provided.

In Inama, a molecular weight of a ligand is 50,000 or less, and a range of a negative functional group is provided (See Inama; Paragraphs [0009] and [0014]). Furthermore, Applicant notes that Inama teaches that "the molecular weight of a ligand may be any and especially regulation is unnecessary." (See Inama; Paragraph [0009] of Machine Translation). Kuroda '449 also teaches that "there is no particular restriction with respect to the molecular weight of the ligands." (See Kuroda '449; Col. 8, lines 6-7) Therefore, Inama and Kuroda '449 teaches that the molecular weight of a ligand generally does not matter such that those references clearly lack the recognition of a ratio between the amounts of tryptophan and polyanionic compound as a result-effective variable.

As discussed above, the characterization of routine experimentation can only be asserted if the relationship of a molar ratio between amounts of tryptophan and polyanionic compounds is recognized by the prior art as the result-effective variable.

Recognition of the relationship between the two amounts of immobilized compounds is essential to the obviousness of conducting experiments to determine the optimum values for improving the adsorbent. Importantly, the recognition that the ratio of amounts between compounds is the result-effective variable which Applicant has discovered and claimed is neither disclosed nor suggested in the references.

The mere disclosure of molecular weight ranges for two compounds shows no insight or understanding of the criticality of the ratio of amounts between the two compounds. The disclosure of ranges in an average molecular weight of tryptophan is provided independently of the range of average molecular weight of polyanion compounds. Therefore, any molecular weight varied within those ranges is chosen independently, without regard to a ratio between the two compounds. Thus, the references simply provide ranges for tryptophan and polyanion compounds in a vacuum, without the disclosure of any relationship between the two. Therefore, optimization of each of the compounds is done independently, without recognition or understanding of how variation in one compound affects the other.

For example, one of ordinary skill may by happenstance adjust the amount of each compound individually to achieve the molar ratio claimed by Applicant. Even so, one of ordinary skill would do so based on the adjustment of the two parameters individually without the understanding that the molar ratio is the crucial parameter to be adjusted. Simply because one may fortuitously adjust the amounts of individual compounds to achieve the claimed ratio does not provide the necessary recognition of that ratio as the result-effective variable. This distinction is crucial. Without the recognition of Applicant's parameter as a result-effective variable, optimization of that variable is not obvious.

Thus, one of ordinary skill in the art could not determine the optimum or workable ranges of a result-effective variable as a matter of routine experimentation since the result-effective variable of a molar ratio of an amount of tryptophan derivative to

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polyanionic compound is clearly not recognized in the prior art as achieving the result of removing fibrinogen and low-density lipoprotein.

In contrast, the present invention requires the molar ratio of the amount of the immobilized tryptophan derivative to the amount of the immobilized polyanionic compound to be 1 to 70. This feature provides the benefit of a high blood cell passing property along with a high adsorption ability (See Specification; Page 14, lines 3-14).

Thus, Inama, Tani and Kuroda '449 do not disclose or suggest this feature of the present invention as required by independent Claim 1. The ancillary references do not remedy the deficiencies of Inama, Tani and Kuroda '449.

Since the applied references fail to disclose, teach or suggest the above features recited in independent Claim 1, those references cannot be said to anticipate nor render obvious the invention which is the subject matter of that claim.

Accordingly, independent Claim 1 is believed to be in condition for allowance and such allowance is respectfully requested.

The remaining claims depend either directly or indirectly from independent Claim 1 and recite additional features of the invention which are neither disclosed nor fairly suggested by the applied references and are therefore also believed to be in condition for allowance and such allowance is respectfully requested.

### Conclusion

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los

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Angeles, California telephone number (310) 785-4721 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,

HOGAN & HARTSON L.L.P.

Date: March 12, 2009

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